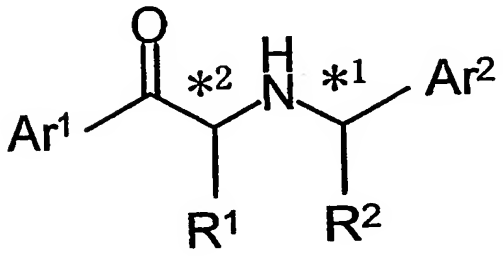
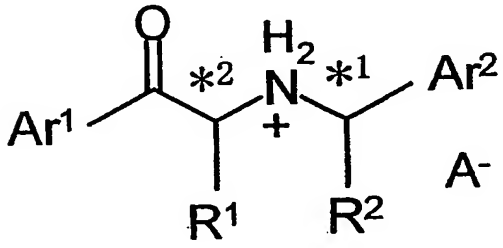
CLAIMS

1. A process for producing an optically active α-substituted aminoketone represented by formula (4):



(4)

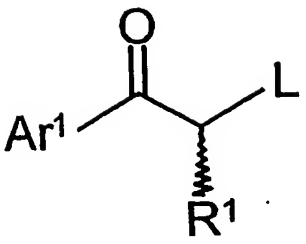
(wherein Ar^1 and Ar^2 each independently represent a substituted or unsubstituted C_6-C_{15} aryl group, R^1 represents a C_1-C_{12} alkyl or C_7-C_{12} aralkyl group, R^2 represents a C_1-C_{12} alkyl group, *1 and *2 each represent an asymmetric carbon atom) or an optically active α-substituted aminoketone salt represented by formula (5):



(5)

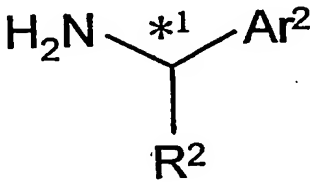
(wherein Ar^1, Ar^2, R^1, R^2, *1, and *2 are the same as above, and A^- represents a counter anion), the process comprising the steps of:

reacting an α-substituted ketone represented by formula (1):



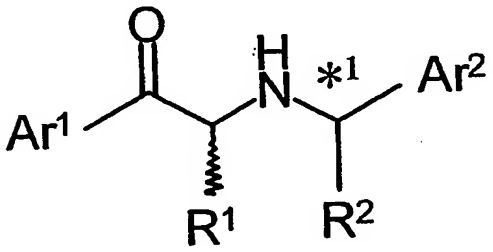
(1)

(wherein Ar^1 and R^1 are the same as above, and L represents a leaving group) with an optically active amine represented by formula (2):



(2)

(wherein Ar^2, R^2, and *1 are the same as above) to yield a mixture of diastereomers of an optically active α-substituted aminoketone represented by formula (3):



(3)

(wherein Ar^1, Ar^2, R^1, R^2, and *1 are the same as above); and

isolating one diastereomer from the mixture after optionally yielding salts of the diastereomers with an acid.

2. The process according to claim 1, wherein L is a halogen atom.

3. The process according to claim 2, wherein the halogen atom is a chlorine atom or bromine atom.

4. The process according to any one of claims 1 to 3 wherein Ar^2 is a phenyl group or a p-methoxyphenyl group; and R^2 is a methyl group.

5. The process according to any one of claims 1 to 4, wherein R^1 is a methyl group or an ethyl group.

6. The process according to any one of claims 1 to 5, wherein, in the step of isolating the diastereomer from the mixture of the diastereomers of the optically active α-substituted aminoketone represented by formula (3), a crystallization method, a chromatographic method, or a distillation method is employed.

7. The process according to any one of claims 1 to 5, wherein, in the step of isolating the diastereomer from the mixture of the diastereomers of the optically active α-substituted aminoketone represented by formula (3), the salts of the diastereomers with the acid are yielded, and the salt of one diastereomer is preferentially crystallized from a solvent.

8. The process according to claim 7, wherein the acid is sulfonic acid.

9. The process according to claim 8, wherein the sulfonic acid is methanesulfonic acid.

10. The process according to any one of claims 7 to 9, wherein the solvent is at least one selected from the group consisting of ester solvents, ether solvents, ketone solvents, halogenated solvents, alcohol solvents, hydrocarbon solvents, nitrile solvents, and water.

11. The process according to any one of claims 7 to 9, wherein the solvent is ethyl acetate, acetone, or dimethoxyethane.

12. The process according to any one of claims 1 to 11, wherein, in formula (4) or (5), the absolute configuration at *2 is S and the absolute configuration at *1 is R; or the absolute configuration at *2 is R and the absolute configuration at *1 is S.

13. The process according to claim 7, wherein the acid is hydrogen halide.

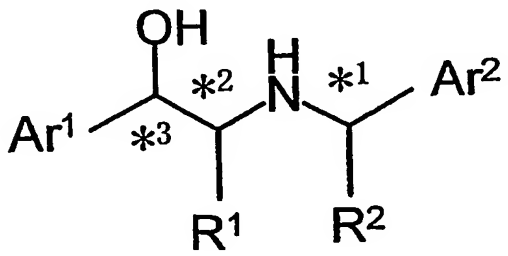
14. The process according to claim 13, wherein the hydrogen halide is hydrogen chloride or hydrogen bromide.

15. The process according to claim 7, 13, or 14, wherein the solvent is an alcohol solvent or water.

16. The process according to claim 7, 13, or 14, wherein the solvent is ethanol or a mixture of ethanol and water.

17. The process according to any one of claims 13 to 16, wherein, in formula (4) or (5), the absolute configuration at *2 is R and the absolute configuration at *1 is R; or the absolute configuration at *2 is S and the absolute configuration at *1 is S.

18. A process for producing an optically active β-substituted amino alcohol represented by formula (6) or a salt thereof:



(6)

(wherein Ar^1, Ar^2, R^1, R^2, *1, and *2 are the same as above, and *3 represents an asymmetric carbon atom), comprising a step of stereoselectively reducing an optically active α-substituted aminoketone represented by formula (4) above or an optically active α-substituted aminoketone salt represented by formula (5) above produced by the process of claim 1.

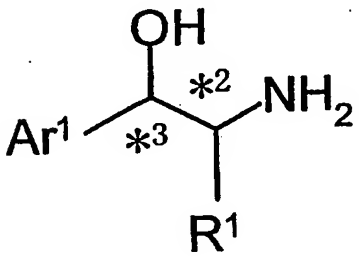
19. The process according to claim 18, wherein the anti-isomer is selectively reduced using a boron compound in methanol, ethanol, or a mixture of ethanol and water.

20. The process according to claim 19, wherein the boron

compound is sodium borohydride.

21. The process according to any one of claims 18 to 20, wherein, in formula (6), the absolute configuration at *2 is S, the absolute configuration at *1 is R, and the absolute configuration at *3 is R; the absolute configuration at *2 is R, the absolute configuration at *1 is R, and the absolute configuration at *3 is S; the absolute configuration at *2 is R, the absolute configuration at *1 is S, and the absolute configuration at *3 is S; or the absolute configuration at *2 is S, the absolute configuration at *1 is S, and the absolute configuration at *3 is R.

22. A process for producing an optically active β-amino alcohol represented by formula (7) or a salt thereof:

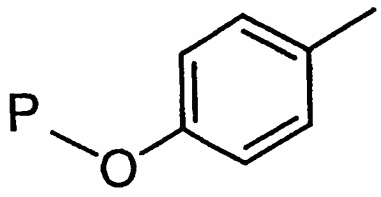


(7)

(wherein Ar^1, R^1, *2, and *3 are the same as above), comprising the step of hydrogenolyzing an optically active β-substituted amino alcohol represented by formula (6) or a salt thereof produced by the process of claim 18.

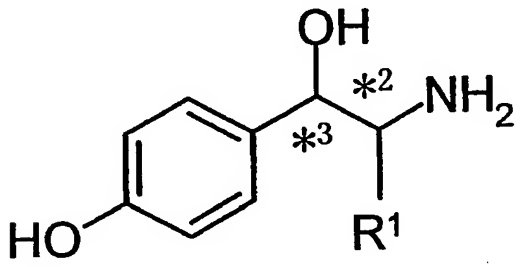
23. The process according to claim 22, wherein, in

formula (6), Ar^1 is a p-hydroxyphenyl group or a hydroxyl-protected p-hydroxyphenyl group represented by formula (10):



(10)

(wherein P represents a hydrogen atom or a protecting group protecting the hydroxyl group), and an optically active β-amino alcohol represented by formula (9) or a salt thereof:



(9)

(wherein R^1, *2, and *3 are the same as above) is produced by the hydrogenolysis after optionally removing the protecting group protecting the hydroxyl group.

24. The process according to claim 23, wherein P represents a benzyl-type protecting group, an aroyl-type protecting group, or a sulfonyl-type protecting group.

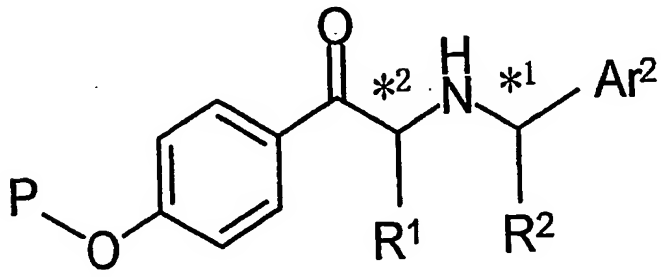
25. The process according to any one of claims 22 to 24, wherein, in formula (9), the absolute configuration at *2 is S and the absolute configuration at *3 is R; or the absolute configuration at *2 is R and the absolute configuration at *3 is S.

26. A process of producing an optically active β-amino alcohol represented by formula (7) above or a salt thereof, wherein an optically active α-substituted aminoketone represented by formula (4) above or an optically active α-substituted aminoketone salt represented by formula (5) above is stereoselectively reduced while simultaneously performing the hydrogenolysis.

27. The process according to claim 26, wherein the anti-isomer is selectively reduced by hydrogenation in the presence of a transition metal catalyst while simultaneously performing the hydrogenolysis.

28. The process according to claim 27, wherein the transition metal catalyst comprises palladium-carbon or palladium(II) hydroxide-carbon.

29. The process according to any one of claims 26 to 28, wherein an optically active α-substituted aminoketone represented by formula (11) or a salt thereof:



(11)

(wherein R^1, R^2, Ar^2, *1, *2, and P are the same as above) is stereoselectively reduced while simultaneously performing

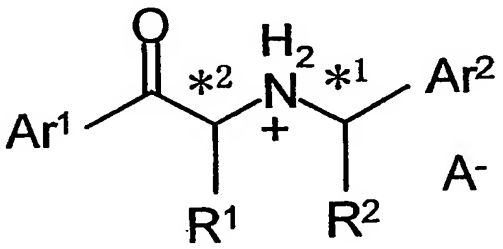
the hydrogenolysis after removing the protecting group protecting the hydroxyl group to yield an optically active β-amino alcohol represented by formula (9) above or a salt thereof.

30. The process according to claim 29, wherein P is a benzyl-type protecting group, an aroyl-type protecting group, or a sulfonyl-type protecting group.

31. The process according to any one of claims 26 to 30, wherein in formula (9), the absolute configuration at *2 is S and the absolute configuration at *3 is R; or the absolute configuration at *2 is R and the absolute configuration at *3 is S.

32. The process according to any one of claims 26 to 31, wherein the optically active α-substituted aminoketone represented by formula (4) or the optically active α-substituted aminoketone salt represented by formula (5) produced by the process of claim 1 is used as the starting material.

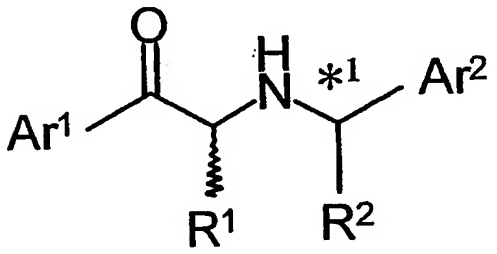
33. A process for isolating an optically active α-substituted aminoketone salt represented by formula (5):



(5)

(wherein Ar^1 and Ar^2 each independently represent a substituted or unsubstituted C_6-C_{15} aryl group, R^1 represents a C_1-C_{12} alkyl or C_7-C_{12} aralkyl group, R^2 represents a C_1-C_{12} alkyl group, *1 and *2 each represent an asymmetric carbon atom, and A^- represents a counter anion), comprising the steps of:

yielding salts from an acid and a mixture of diastereomers of an optically active α-substituted aminoketone represented by formula (3):



(3)

(wherein Ar^1, R^1, R^2, Ar^2, and *1 are the same as above); and preferentially crystallizing the salt of one diastereomer from a solvent.

34. The isolation process according to claim 33, wherein the acid is sulfonic acid.

35. The isolation process according to claim 34, wherein the sulfonic acid is methanesulfonic acid.

36. The isolation process according to claim 34 or 35, wherein the solvent is at least one selected from ester solvents, ether solvents, ketone solvents, halogenated solvents, alcohol solvents, hydrocarbon solvents, nitrile

solvents, and water.

37. The isolation process according to claim 34 or 35, wherein the solvent is ethyl acetate, acetone, or dimethoxyethane.

38. The isolation process according to any one of claims 34 to 37, wherein, in formula (5), the absolute configuration at *2 is S and the absolute configuration at *1 is R; or the absolute configuration at *2 is R and the absolute configuration at *1 is S.

39. The isolation process according to claim 33, wherein the acid is hydrogen halide.

40. The isolation process according to claim 39, wherein the hydrogen halide is hydrogen chloride or hydrogen bromide.

41. The isolation process according to claim 39 or 40, wherein the solvent is an alcohol solvent or water.

42. The isolation process according to claim 39 or 40, wherein the solvent is ethanol or a mixture of ethanol and water.

43. The isolation process according to any one of claims 39 to 42, wherein, in formula (5), the absolute configuration at *2 is R and the absolute configuration at *1 is R; or the absolute configuration at *2 is S and the absolute configuration at *1 is S.

44. The isolation process according to any one of claims 33 to 43, wherein Ar^2 is a phenyl group or a p-methoxyphenyl

group; and R^2 is a methyl group.

45. The isolation process according to any one of claims 33 to 44, wherein R^1 is a methyl group or an ethyl group.

46. The isolation process according to any one of claims 33 to 45, wherein Ar^1 is a phenyl group, a p-hydroxyphenyl group, a p-benzyloxyphenyl group, p-benzoyloxyphenyl group, or a p-methanesulfonyloxyphenyl group.

47. An optically active α-substituted aminoketone represented by formula (4) above wherein R^1 is a C_1-C_4 alkyl group or a C_7-C_{12} aralkyl group, or an optically active α-substituted aminoketone salt represented by formula (5) above wherein R^1 is a C_1-C_4 alkyl group or a C_7-C_{12} aralkyl group.

48. The optically active α-substituted aminoketone or the optically active α-substituted aminoketone salt according to claim 47, wherein, in formula (4) or (5), Ar^2 is a phenyl or p-methoxyphenyl group, and R^2 is a methyl group.

49. The optically active α-substituted aminoketone or the optically active α-substituted aminoketone salt according to claim 47 or 48, wherein, in formula (4) or (5), R^1 is a methyl group or an ethyl group.

50. The optically active α-substituted aminoketone or the optically active α-substituted aminoketone salt according to any one of claims 47 to 49, wherein, in formula (4) or (5), Ar^1 is a phenyl group, a p-hydroxyphenyl group, a p-

benzyloxyphenyl group, p-benzoyloxyphenyl group, or a p-methanesulfonyloxyphenyl group.

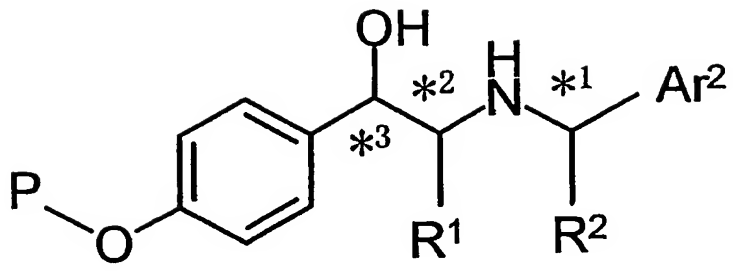
51. The optically active α-substituted aminoketone or the optically active α-substituted aminoketone salt according to any one of claims 47 to 50, wherein, in formula (4) or (5), the absolute configuration at *2 is S and the absolute configuration at *1 is R; or the absolute configuration at *2 is R and the absolute configuration at *1 is S.

52. The optically active α-substituted aminoketone salt according to any one of claims 47 to 51, wherein A^- in formula (5) is a methanesulfonate ion.

53. The optically active α-substituted aminoketone or the optically active α-substituted aminoketone salt according to any one of claims 47 to 50, wherein, in formula (4) or (5), the absolute configuration at *2 is R and the absolute configuration at *1 is R; or the absolute configuration at *2 is S and the absolute configuration at *1 is S.

54. The optically active α-substituted aminoketone salt according to any one of claims 47 to 50 and 53, wherein A^- in formula (5) is a chlorine ion or a bromine ion.

55. An optically active β-substituted amino alcohol represented by formula (8) or a salt thereof:



(8)

(wherein R^1 represents a C_1-C_{12} alkyl or C_7-C_{12} aralkyl group, Ar^2 represents a substituted or unsubstituted C_6-C_{15} aryl group, R^2 represents a C_1-C_{12} alkyl group, *1, *2, and *3 each represent an asymmetric carbon atom, and P represents a hydrogen atom or a protecting group protecting the hydroxyl group).

56. The optically active β-substituted amino alcohol or the salt thereof according to claim 55, wherein Ar^2 is a phenyl group or a p-methoxyphenyl group, and R^2 is a methyl group.

57. The optically active β-substituted amino alcohol or the salt thereof according to claim 55 or 56, wherein R^1 is a methyl group or an ethyl group.

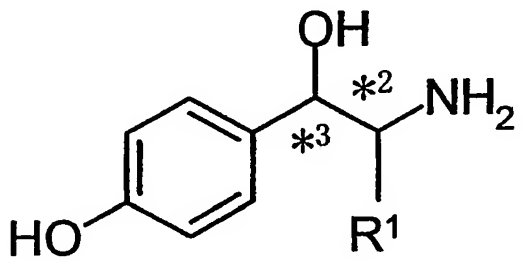
58. The optically active β-substituted amino alcohol or the salt thereof according to any one of claims 55 to 57, wherein P is a benzyl-type protecting group, an aroyl-type protecting group, or a sulfonyl-type protecting group.

59. The optically active β-substituted amino alcohol or the salt thereof according to any one of claims 55 to 57,

wherein P is a benzyl group, an benzoyl group, or a methanesulfonyl group.

60. The optically active β-substituted amino alcohol or the salt thereof according to any one of claims 55 to 59, wherein, in formula (8), the absolute configuration at *2 is S, the absolute configuration at *1 is R, and the absolute configuration at *3 is R; the absolute configuration at *2 is R, the absolute configuration at *1 is R, and the absolute configuration at *3 is S; the absolute configuration at *2 is R, the absolute configuration at *1 is S, and the absolute configuration at *3 is S; or the absolute configuration at *2 is S, the absolute configuration at *1 is S, and the absolute configuration at *3 is R.

61. A process for isolating an optically active β-amino alcohol represented by formula (9) or a salt thereof with an optically inactive acid:



(9)

(wherein R^1 represents a C_1-C_{12} alkyl or C_7-C_{12} aralkyl group, and *2 and *3 each represent an asymmetric carbon atom), comprising a step of crystallizing the optically active β-

amino alcohol represented by formula (9) or the salt thereof with the optically inactive acid from an alcohol solvent to remove impurities contained therein to the mother liquor to thereby obtain crystals of the optically active β-amino alcohol represented by formula (9) or the salt thereof with the optically inactive acid.

62. The isolation process according to claim 61, wherein R^1 is a methyl group or an ethyl group.

63. The isolation process according to claim 61 or 62, wherein the alcohol solvent is methanol, ethanol, or isopropanol.

64. The isolation process according to any one of claims 61 to 63, wherein an auxiliary solvent is used to improve at least one of the yield of the compound represented by formula (9) above, the process concentration, the liquid properties, and the physical properties of the crystals obtained.

65. The isolation process according to claim 64, wherein the auxiliary solvent is at least one selected from the group consisting of ester solvents, ether solvents, ketone solvents, halogenated solvents, hydrocarbon solvents, and nitrile solvents.

66. The isolation process according to claim 64, wherein the auxiliary solvent is ethyl acetate or methylene chloride.

67. The isolation process according to any one of claims

64 to 66, wherein the volume ratio of the auxiliary solvent to the alcohol solvent upon completion of the process for crystallization is 1 or more.

68. The isolation process according to any one of claims 61 to 67, wherein, the compound represented by formula (9) has the S absolute configuration at *2 and the R absolute configuration at *3 and the impurity to be removed is either its diastereomer (having the S absolute configuration at *2 and the S absolute configuration at *3) or its enantiomer (having the R absolute configuration at *2 and the S absolute configuration at the *3); or the compound represented by formula (9) has the R absolute configuration at *2 and the S absolute configuration at *3 and the impurity to be removed is either its diastereomer (having the R absolute configuration at *2 and the R absolute configuration at *3) or its enantiomer (having the S absolute configuration at *2 and the R absolute configuration at the *3).

69. The isolation process according to any one of claims 61 to 68, wherein the optically active β-amino alcohol represented by (9) produced by the method of claim 23 or 29 is used as a starting material.

70. The isolation process according to any one of claims 61 to 69, wherein the optically inactive acid is hydrogen chloride, hydrogen bromide, or methanesulfonic acid.